Complete Summary

GUIDELINE TITLE

Public health guidance for community-level preparedness and response to severe acute respiratory syndrome (SARS). Version 2. Supplement F: laboratory guidance.

BIBLIOGRAPHIC SOURCE(S)

Centers for Disease Control and Prevention (CDC). Public health guidance for community-level preparedness and response to severe acute respiratory syndrome (SARS). Version 2. Supplement F: laboratory guidance. Atlanta (GA): Centers for Disease Control and Prevention (CDC); 2004 Jan 8. 32 p.

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

Severe acute respiratory syndrome (SARS)

GUIDELINE CATEGORY

Diagnosis
Management

CLINICAL SPECIALTY

Pathology
Preventive Medicine

INTENDED USERS

Public Health Departments

GUIDELINE OBJECTIVE(S)

- To provide ready access to high-quality severe acute respiratory syndrome-associated coronavirus (SARS-CoV) laboratory diagnostics for the public health community
- To ensure that SARS-CoV laboratory diagnostics are used safely and appropriately and that results are interpreted appropriately

TARGET POPULATION

Persons potentially infected with severe acute respiratory syndrome-associated coronavirus (SARS-CoV)

INTERVENTIONS AND PRACTICES CONSIDERED

Diagnostic Assays

1. Real-time reverse-transcription polymerase chain reaction (RT-PCR) assays
2. Antibody (serologic) assays
3. Other assays, such as cell culture (not recommended), electron microscopy, and immunohistologic or in situ probe hybridization studies

Centers for Disease Control and Prevention Laboratory Diagnostics Plan

1. Assay deployment
2. Proficiency testing
3. Assessment of laboratory preparedness
4. Confirmatory testing
5. Specimen collection and handling
6. Informed consent
7. Evaluation of assay sensitivity
8. Test interpretation
9. Data reporting and integration
10. Training and education

MAJOR OUTCOMES CONSIDERED

Sensitivity and specificity of laboratory diagnostics in detecting and documenting severe acute respiratory syndrome-associated coronavirus (SARS-CoV) disease

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Not stated

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Not stated

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Not applicable

METHODS USED TO ANALYZE THE EVIDENCE

Review

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

The guideline was prepared by the Centers for Disease Control and Prevention's (CDC) Severe Acute Respiratory Syndrome (SARS) Preparedness Committee, which was assembled to prepare for the possibility of future SARS outbreaks. The Committee includes eight working groups, each of which addressed a component of SARS preparedness and response. The working groups derived the guidance document from lessons learned during the 2003 epidemic, other CDC preparedness and response plans, and the advice, suggestions, and comments of state and local health officials and representatives of professional organizations, convened by means of teleconferences and meetings. Meetings were held on August 12-13, 2003 (public health preparedness and response), September 12, 2003 (preparedness in healthcare facilities), and September 18, 2003 (laboratory diagnostics).

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

This is an updated version of the draft guidance document issued by the Centers for Disease Control and Prevention (CDC) on November 3, 2003. CDC revised the draft based on comments received from public health partners, healthcare providers, professional organizations, and others.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Priority Activities

- Improve the ability to detect severe acute respiratory syndrome-associated coronavirus (SARS-CoV) infection by optimizing the selection and timing of specimen collection and processing.
- Provide SARS-CoV assays for reverse-transcription-polymerase chain reaction (RT-PCR) testing to Laboratory Response Network (LRN) laboratories and for serologic testing to state public health laboratories.
- Distribute proficiency panels and questionnaires to participating laboratories to determine the ability of laboratories to provide valid SARS-CoV diagnostics.
- Provide guidance on laboratory safety for SARS-CoV and other respiratory diagnostic testing and for possible SARS-CoV-containing specimens submitted for other tests.
- Provide guidance for interpreting test results, taking into account the potential for false-positive and false-negative results and the availability of applicable clinical and epidemiologic information.
- Identify surge capacity for laboratory testing in the event of a large severe acute respiratory syndrome (SARS) outbreak.

CDC's Laboratory Diagnostics Plan

The Center for Disease Control and Prevention (CDC) is planning and embarking on a range of laboratory diagnostics activities that will enhance the capacity to detect a reappearance of SARS-CoV and respond to and manage outbreaks. Objectives and descriptions of these activities are as follows.

Objective 1: Expand public health access to high-quality SARS-CoV diagnostics.

Activities

- Assay deployment: CDC has deployed the SARS-CoV RT-PCR diagnostic assay under an Investigative Device Exemption (IDE) from the Food and Drug Administration (FDA). Protocols for both the RT-PCR and the serologic assay have been approved by CDC's Institutional Review Board (IRB). RT-PCR assays were deployed through the Laboratory Response Network to selected

laboratories in nearly all states; serologic assays have been deployed to nearly all state public health laboratories.

- Proficiency testing: To assess the availability and quality of SARS-CoV diagnostics in laboratories that received CDC's RT-PCR and antibody assays, CDC will distribute a panel of positive and negative specimens for testing (proficiency panels). The receiving laboratories will test these specimens and send their results to CDC for analysis of findings and responses to a questionnaire. These data will provide information on the laboratory's readiness to perform SARS-CoV diagnostics (see Appendix F1 in original guideline document).
- Assessment of SARS-CoV diagnostics in non-public health laboratories: Determining the availability and quality of SARS-CoV testing in non-public health laboratories will provide an assessment of overall laboratory diagnostic preparedness. Several clinical pathology professional organizations conduct laboratory surveys and distribute proficiency panels. CDC will assist with SARS surveys and provide proficiency panels so that the professional organizations can assess the status of SARS-CoV diagnostics in their members' laboratories.
- Confirmatory testing: Positive RT-PCR test results should be confirmed in a reference laboratory. Confirmatory testing is particularly important in areas with a low prevalence of SARS-CoV disease, where the positive predictive value of the assay is likely to be quite low. CDC will conduct confirmatory testing during the early phases of an outbreak. Other laboratories that are proficient in SARS-CoV diagnostics will participate in confirmatory testing as outbreaks escalate. Early in an outbreak, positive serologic tests should also be confirmed; later tests conducted in a proficient laboratory do not required confirmation.

  A key factor in the value of confirmatory RT-PCR testing is specimen handling. To interpret confirmatory test results, the aliquot of the specimen submitted for testing should not have been at risk for template contamination or degradation. The approach for and interpretation of confirmatory testing must consider all potential sources and types of template contamination (e.g., whole viral genome, genome portions, PCR products). Guidelines for confirmatory testing are provided in Appendix F2 in original guideline document.

Objective 2: Improve the ability to detect SARS-CoV by optimizing the selection and timing of specimen collection and processing.

Most patients in the early stages of SARS-CoV disease have a low titer of virus in respiratory and other secretions and require time to mount an antibody response. In one study (in patients treated with high-dose steroids and ribavirin), nasopharyngeal (NP) aspirates were found to be PCR positive in <40% of patients during the first week of illness and in >50% of patients during the second week of illness (Peiris 2003). During the second week of illness, stool specimens were found to be PCR positive in a higher percentage of patients than were nasopharyngeal aspirates. Limited data suggest that serum may be the best specimen for SARS-CoV PCR diagnostics during the first few days of illness.

Activities

- Specimen collection: CDC has developed guidance for health departments and laboratorians to maximize the efficiency and accuracy of diagnostic procedures. Clinicians and laboratorians are asked to:
    - Obtain informed consent: A signed consent form is recommended for RT-PCR and enzyme immunoassays (EIA) testing because neither assay has been licensed by the FDA and the RT-PCR test is being used under an FDA-approved Investigative Device Exemption. In addition, a signed consent form is required to store specimen remainders for future investigations (see Appendix F3 in original guideline document).
    - Collect multiple specimens: The type and timing of specimen collection is important to maximize the probability of detecting evidence of SARS-CoV infection. Since it is not yet clear which specimen type is best for detecting viral ribonucleic acid (RNA), it is important to collect different types of specimens and at multiple times during the illness. Appendix F4 in the original guideline document provides guidance on the type and timing of specimens for SARS-CoV diagnostics.
    - Handle specimens correctly: CDC has developed guidance for specimen collection, handling, and shipping (Appendix F4 in original guideline document). State and local health departments can use these guidelines to educate clinicians on appropriate methods of specimen management.
- Assay sensitivity: CDC will evaluate ways to improve assay sensitivity, such as extracting RNA from a larger volume of the specimen and including a larger amount of template RNA in the RT-PCR reaction. CDC is developing immunoglobulin G (IgG) and immunoglobulin M (IgM) assays using expressed proteins as the antigens. Preliminary data suggest that antibody assays using the SARS-CoV S protein might detect an antibody response earlier in illness.

Objective 3: Ensure that SARS-CoV specimens are handled safely and that SARS-CoV diagnostic tests are used and interpreted appropriately.

Activities

- Biosafety guidance: The laboratory-acquired SARS-CoV infection in Singapore (Singapore Ministry of Health 2003) and presumed laboratory-acquired SARS-CoV infection in Taiwan (Department of Health, Taiwan 2003) underscore the need to handle SARS-CoV specimens and SARS-CoV-infected tissue culture material safely. CDC has developed guidelines for handling these types of specimens and materials (Appendix F5 in original guideline document) and for implementing a surveillance program in the event of a laboratory exposure (Appendix F6 in original guideline document). State and local health departments can use these guidelines to educate personnel in viral diagnostic, research, and clinical laboratories about safe specimen handling and appropriate responses to a laboratory exposure.
- Test interpretation: Clinicians should interpret SARS-CoV test results in consultation with state or local health department officials and with consideration of data on the clinical and epidemiologic features of the illness and the type and timing of specimen collection. CDC has developed guidelines to guide state and local health department staff in their consultations with clinicians about test interpretation (Appendix F7 in original guideline document). CDC, in cooperation with the Council of State and Territorial

Epidemiologists (CSTE), has also developed criteria for laboratory diagnosis of SARS-CoV infection (Appendix F8 in original guideline document).

- Data reporting and integration: State and local health departments will collect clinical and epidemiologic data on potential cases of SARS-CoV disease and report cases to CDC through a web-based reporting system. CDC will send laboratory data back to state and local health departments daily. The clinical and epidemiologic information reported to CDC and downloaded back to the states can provide a source of patient information that can help laboratorians consider appropriate testing strategies and interpret test results. With guidance from state and local health departments, CDC will facilitate access to data as requested. In addition, results of laboratory testing on any specimens submitted to CDC will be integrated into the data provided to state and local health departments, allowing timely dissemination of this information.
- Training and education: Diagnostic assays have an important role in detecting an introduction of SARS-CoV, managing a SARS outbreak, and addressing concerns about SARS. The healthcare and public health communities should be aware of the value, limitations, and appropriate use and interpretation of SARS-CoV diagnostics. CDC will provide training and educational materials that state and local health departments can use to educate clinicians and public health workers about SARS-CoV diagnostics.
- Coordination: Coordinated information sharing among clinicians, laboratorians, and epidemiologists is central to efficient investigation of potential cases of SARS-CoV disease. CDC will assist public health laboratories and epidemiologists in developing rapid and coordinated strategies for: 1) collecting, tracking, and testing specimens, 2) interpreting test results, 3) reporting information to clinicians, and 4) communicating results to CDC, other public health officials, and the public.

Objective 4: Ensure the availability of SARS-CoV diagnostic test kits and protocols for testing other respiratory pathogens.

Activities

- Diagnostic supplies: The supply of SARS-CoV RT-PCR and serologic test kits is limited. To ensure the availability of a sufficient number of kits to meet routine public health needs and the anticipated high demand associated with simultaneous outbreaks, CDC is monitoring both the deployment and number of kits. After patterns of use have been determined, CDC will plan the production of new kits to ensure that the supply can meet both projected baseline needs and the accelerated use associated with a SARS outbreak.
- Tests for alternative respiratory agents: CDC will complete the development and initial evaluation of real-time PCR assays for the most important common respiratory pathogens in the United States and make primer and probe sequences and protocols available to the Laboratory Response Network and other public health laboratories.

CLINICAL ALGORITHM(S)

The following clinical algorithms are provided in the appendices in the original guideline document:

- SARS-CoV Specimen Testing Guidelines: RT-PCR Testing (Appendix F2)
- RT-PCR Confirmatory Testing (Appendix F2)
- SARS-CoV Specimen Testing Guidelines: Serologic Testing (Appendix F2)
- Serologic Confirmatory Testing (Appendix F2)
- Recommended Specimens for Evaluation of Potential Cases of SARS (Appendix F4)

EVIDENCE SUPPORTING THE RECOMMENDATIONS

REFERENCES SUPPORTING THE RECOMMENDATIONS

References open in a new window

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is not specifically stated for each recommendation. The working groups derived the guidance document from lessons learned during the 2003 epidemic, other Centers for Disease Control and Prevention (CDC) preparedness and response plans, and the advice, suggestions, and comments of state and local health officials and representatives of professional organizations.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Overall

- Ready access to high-quality severe acute respiratory syndrome-associated coronavirus (SARS-CoV) laboratory diagnostics for the public health community
- Safe and appropriate use of SARS-CoV laboratory diagnostics and appropriate interpretation of laboratory results

Specific

- Real-Time RT-PCR Assays. Because real-time reverse-transcription-polymerase chain reaction (RT-PCR) assays use internal probes as well as amplification primers, they can be designed to be very specific for SARS-CoV ribonucleic acid (RNA) (or complementary deoxyribonucleic acid [cDNA]). They can also be very sensitive, with consistent detection limits of between 1 and 10 SARS-CoV RNA copies per reaction. Real-time PCR assays can be performed faster than traditional RT-PCR assays and, because they operate as closed systems, with reduced risk of contamination in the laboratory. Finally, real-time RT-PCR assays can give an accurate estimate of the quantity of virus present in a sample.
- Antibody Assays. The most commonly used serologic assays are based on cultured SARS-CoV antigen as either inactivated whole virus lysate for enzyme immunoassay (EIA) or inactivated virus in cells fixed for immunofluorescence assay (IFA). These assays have proven to be highly

specific, with no cross-reactivity with paired serum specimens from patients infected with the other known human coronaviruses (229E and OC43) or from healthy blood donors and other persons without clinical or epidemiologic evidence of SARS-CoV disease.

POTENTIAL HARMS

The possibility of false-positive and false-negative results with both polymerase chain reaction (PCR) and serologic assays should always be considered when interpreting results; clear strategies to minimize such possibilities and to confirm test results are essential.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

The appendices in the original guideline document provide tools for implementation as follows:

- Appendix F1: Proficiency Testing for Public Health Laboratories Performing SARS-CoV EIA and RT-PCR Diagnostics
- Appendix F2: SARS-CoV Specimen Testing Guidelines: RT-PCR and Serology
- Appendix F3: Guidelines for Clinicians: The Consent Process for SARS-CoV RT-PCR and EIA Testing at CDC and Public Health Laboratories
- Appendix F4: Guidelines for Collecting Specimens from Potential SARS Patients
- Appendix F5: Laboratory Biosafety Guidelines for Handling and Processing Specimens Associated with SARS-CoV
- Appendix F6: Guidelines for Medical Surveillance of Laboratory Personnel Working with SARS-CoV
- Appendix F7: Fact Sheet for Clinicians: Interpreting SARS-CoV Test Results from CDC and Other Public Health Laboratories
- Appendix F8: Guidelines for Laboratory Diagnosis of SARS-CoV Infection

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Getting Better

IOM DOMAIN

Effectiveness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Centers for Disease Control and Prevention (CDC). Public health guidance for community-level preparedness and response to severe acute respiratory syndrome (SARS). Version 2. Supplement F: laboratory guidance. Atlanta (GA): Centers for Disease Control and Prevention (CDC); 2004 Jan 8. 32 p.

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2003 Nov 3 (revised 2004 Jan 8)

GUIDELINE DEVELOPER(S)

Centers for Disease Control and Prevention - Federal Government Agency [U.S.]

SOURCE(S) OF FUNDING

United States Government

GUIDELINE COMMITTEE

Centers for Disease Control and Prevention Severe Acute Respiratory Syndrome (SARS) Preparedness Committee

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Not stated

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Not stated

GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates a previous version issued by the Centers for Disease Control and Prevention (CDC) on November 13, 2003.

GUIDELINE AVAILABILITY

Electronic copies: Available from the Centers for Disease Control and Prevention (CDC) Web site:

- HTML Format
- Microsoft Word
- Portable Document Format (PDF)

Print copies: Available from the Centers for Disease Control and Prevention, MMWR, Atlanta, GA 30333. Additional copies can be purchased from the Superintendent of Documents, U.S. Government Printing Office, Washington, DC 20402-9325; (202) 783-3238.

AVAILABILITY OF COMPANION DOCUMENTS

The following are available:

- In the absence of SARS-CoV transmission worldwide: guidance for surveillance, clinical and laboratory evaluation, and reporting. Atlanta (GA): Centers for Disease Control and Prevention (CDC); 2004 Jan 8. 15 p.

  Electronic copies: Available from the CDC Web site.

- Clinical guidance on the identification and evaluation of possible SARS-CoV disease among persons presenting with community-acquired illness. Atlanta (GA): Centers for Disease Control and Prevention (CDC); 2004 Jan 8. 15 p.

  Electronic copies: Available from the CDC Web site.

- PowerPoint Slide Set: SARS Laboratory Diagnostics Preparedness.

  Electronic copies: Available from the CDC Web site in PDF format and as Microsoft PowerPoint downloads.

- Consent form (SARS-CoV EIA laboratory testing). Atlanta (GA): Centers for Disease Control and Prevention (CDC); 2004 Apr 23. 4 p.

  Electronic copies: Available from the CDC Web site.

- Patient information sheet and consent for long term specimen storage (SARS-Cov EIA testing). Atlanta (GA): Centers for Disease Control and Prevention (CDC); 2004 Apr 24. 3 p.

  Electronic copies: Available from the CDC Web site.

- Patient information sheet and consent for long term specimen storage (SARS laboratory testing: reverse transcription polymerase chain reaction [RT-PCR]). Atlanta (GA): Centers for Disease Control and Prevention (CDC); 2004 Apr 23. 3 p.

  Electronic copies: Available from the CDC Web site.

See also:

- Appendix F1: Proficiency Testing for Public Health Laboratories Performing SARS-CoV EIA and RT-PCR Diagnostics.
- Appendix F2: SARS-CoV Specimen Testing Guidelines: RT-PCR and Serology.

- Appendix F3: Guidelines for Clinicians: The Consent Process for SARS-CoV RT-PCR and EIA Testing at CDC and Public Health Laboratories.
- Appendix F4: Guidelines for Collecting Specimens from Potential SARS Patients.
- Appendix F5: Laboratory Biosafety Guidelines for Handling and Processing Specimens Associated with SARS-CoV.
- Appendix F6: Guidelines for Medical Surveillance of Laboratory Personnel Working with SARS-CoV.
- Appendix F7: Fact Sheet for Clinicians: Interpreting SARS-CoV Test Results from CDC and Other Public Health Laboratories.
- Appendix F8: Guidelines for Laboratory Diagnosis of SARS-CoV Infection.

Electronic copies: Available from the CDC Web site in PDF format and as Microsoft Word downloads.

Print copies: Available from the Centers for Disease Control and Prevention, MMWR, Atlanta, GA 30333. Additional copies can be purchased from the Superintendent of Documents, U.S. Government Printing Office, Washington, DC 20402-9325; (202) 783-3238.

PATIENT RESOURCES

The following is available:

- Information for SARS Patients and Their Close Contacts. Atlanta (GA): Centers for Disease Control and Prevention (CDC); 2004 Feb 6.
- Infection Control Precautions for SARS Patients and Their Close Contacts in Households. Atlanta (GA): Centers for Disease Control and Prevention (CDC); 2004 Jan 8.

Electronic copies: Available from the Centers for Disease Control and Prevention (CDC) Web site.

Print copies: Available from the Centers for Disease Control and Prevention, MMWR, Atlanta, GA 30333. Additional copies can be purchased from the Superintendent of Documents, U.S. Government Printing Office, Washington, DC 20402-9325; (202) 783-3238.

NGC STATUS

This summary was completed by ECRI on February 11, 2004.

COPYRIGHT STATEMENT

Date Modified: 11/1/2004